

Fibroblast activity kills – Circulating endotrophin (PRO-C6) is prognostic for liver-related events in patients with cirrhosis from chronic hepatitis C

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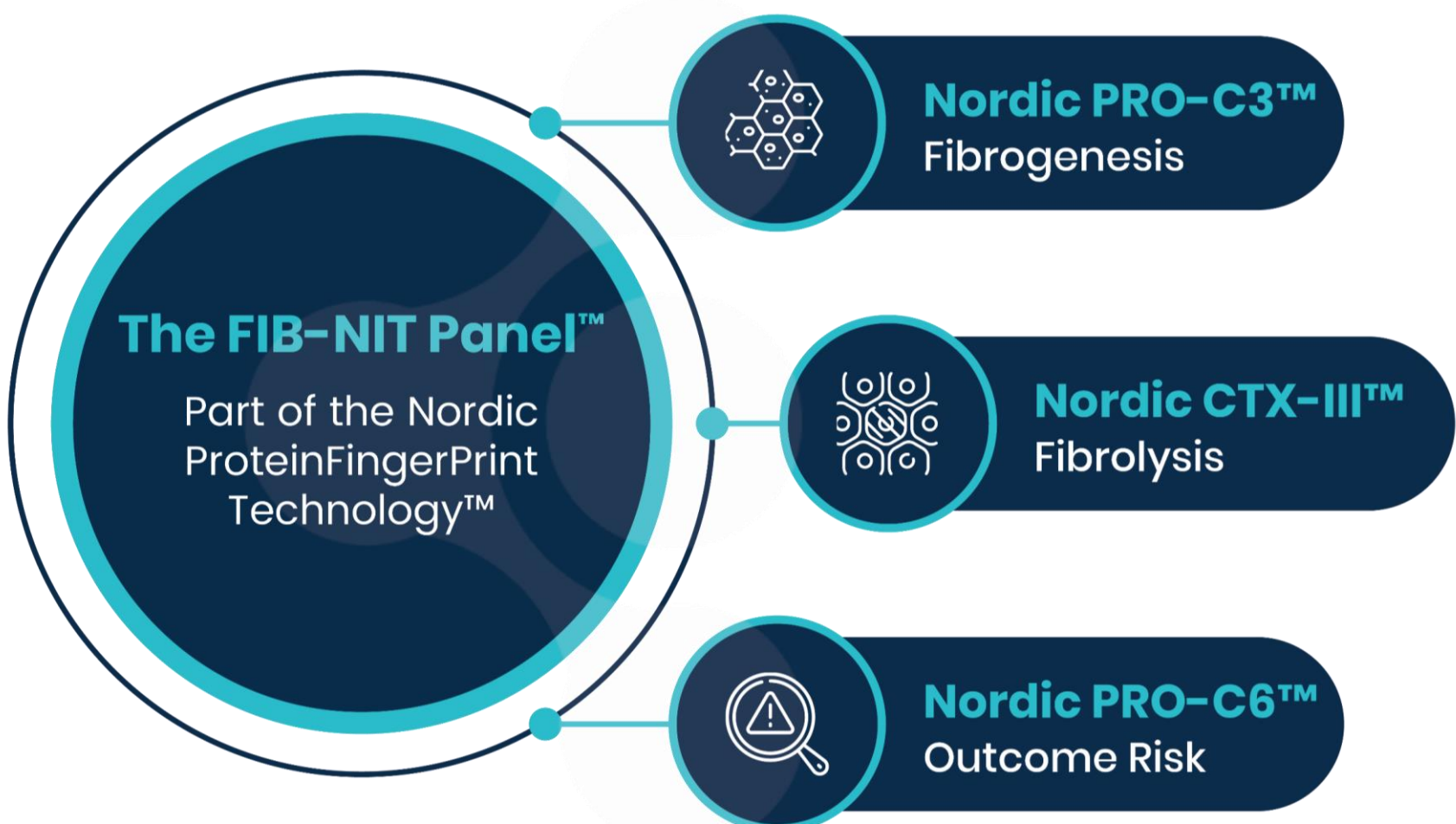
BACKGROUND

Prognostic markers for patients with compensated cirrhosis at increased risk of developing liver-related events are required. Endotrophin, a potential driver of fibroblast activation and mediator of fibroinflammatory disease, can be assessed non-invasively using PRO-C6. Blood-based collagen extracellular matrix remodeling markers may provide novel prognostic information to identify patients with cirrhosis at higher risk of developing a liver-related event.

Our aims were to investigate the ability of PRO-C6 to predict liver-related events in The Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis Trial (HALT-C) (ClinicalTrials.gov #NCT00006164).

METHODS

Our study population included 339 chronic hepatitis C (CHC) patients with and without cirrhosis from HALT-C. NordicPRO-C6™ from The FIB-NIT Panel™, was assessed in serum using a fully validated competitive enzyme-linked immunosorbent assay. Between groups comparison of biomarker levels was performed using Mann-Whitney U test. Quartile-based analysis stratified patients in high and low baseline PRO-C6. Cox proportional hazards regression was used to analyze the prognostic value of serum PRO-C6 to identify patients at risk of developing liver-related events. Data provided by NIDDK CR, a program of the National Institute of Diabetes and Digestive and Kidney Diseases



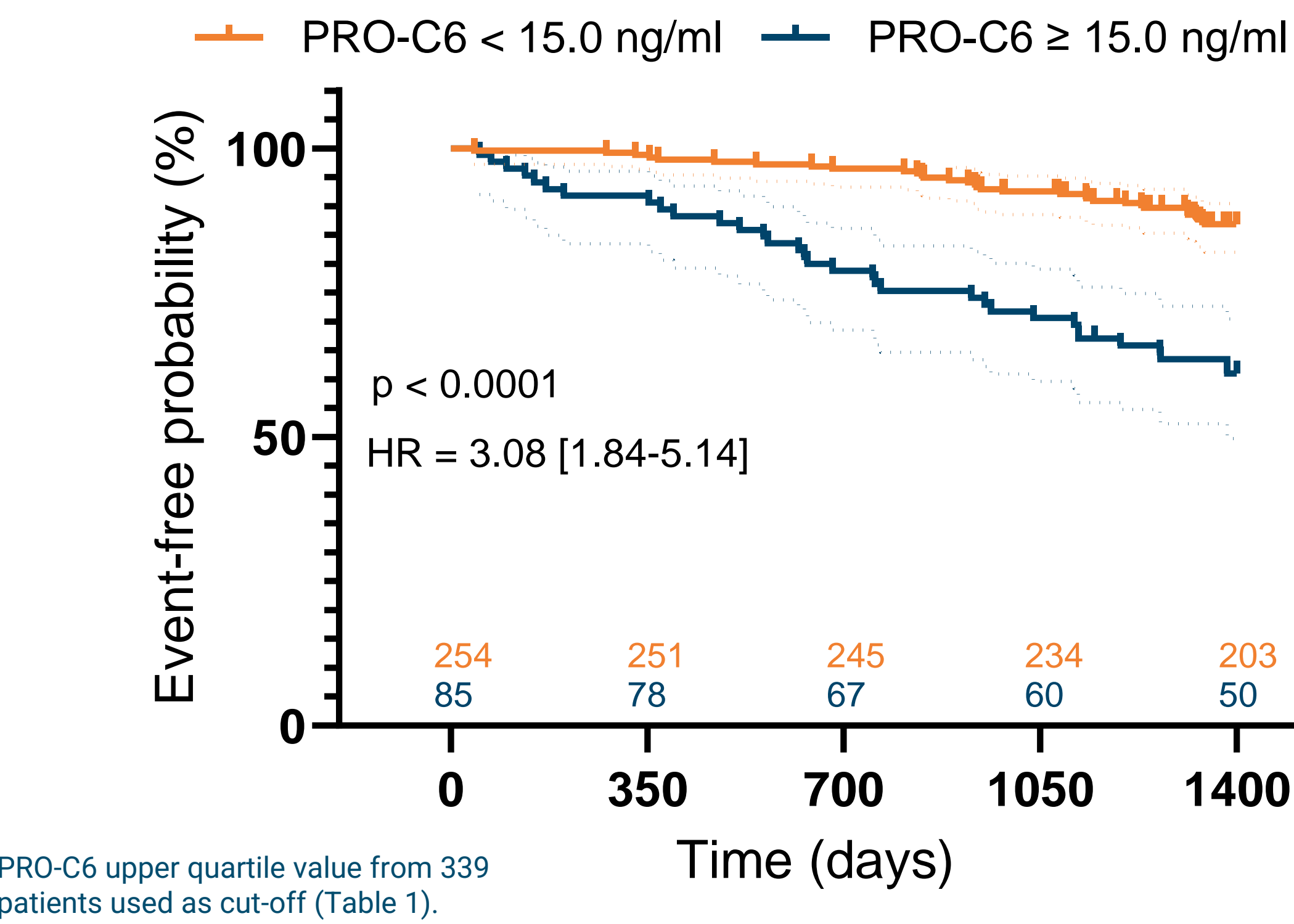
Demographics

Baseline Characteristics	All patients N = 339 ¹	No cirrhosis N = 188 ¹	Cirrhosis N = 151 ¹	p-value ²
Sex, female	109 (32%)	62 (33%)	47 (31%)	0.7
AGE, years	50 (47, 55)	50 (47, 54)	50 (47, 55)	>0.9
BMI, kg/m2	29.4 (26.6, 32.6)	29.5 (26.4, 32.6)	29.3 (26.7, 32.6)	>0.9
Alcohol consumption, life drinks	6,677 (1,095, 20,066)	6,150 (861, 15,924)	7,808 (1,411, 23,574)	0.11
ALT, U/L	87 (61, 129)	86 (57, 124)	90 (65, 133)	0.3
PRO-C6, ng/mL	12.4 (10.0, 15.0)	11.5 (9.6, 14.2)	13.3 (10.7, 17.2)	<0.001
Ishak fibrosis score 0–6, n	0/0/21/109/58/79/72	0/0/21/109/58/0/0	0/0/0/0/0/79/72	<0.001
Liver-related event	66 (19%)	19 (10%)	47 (31%)	<0.001

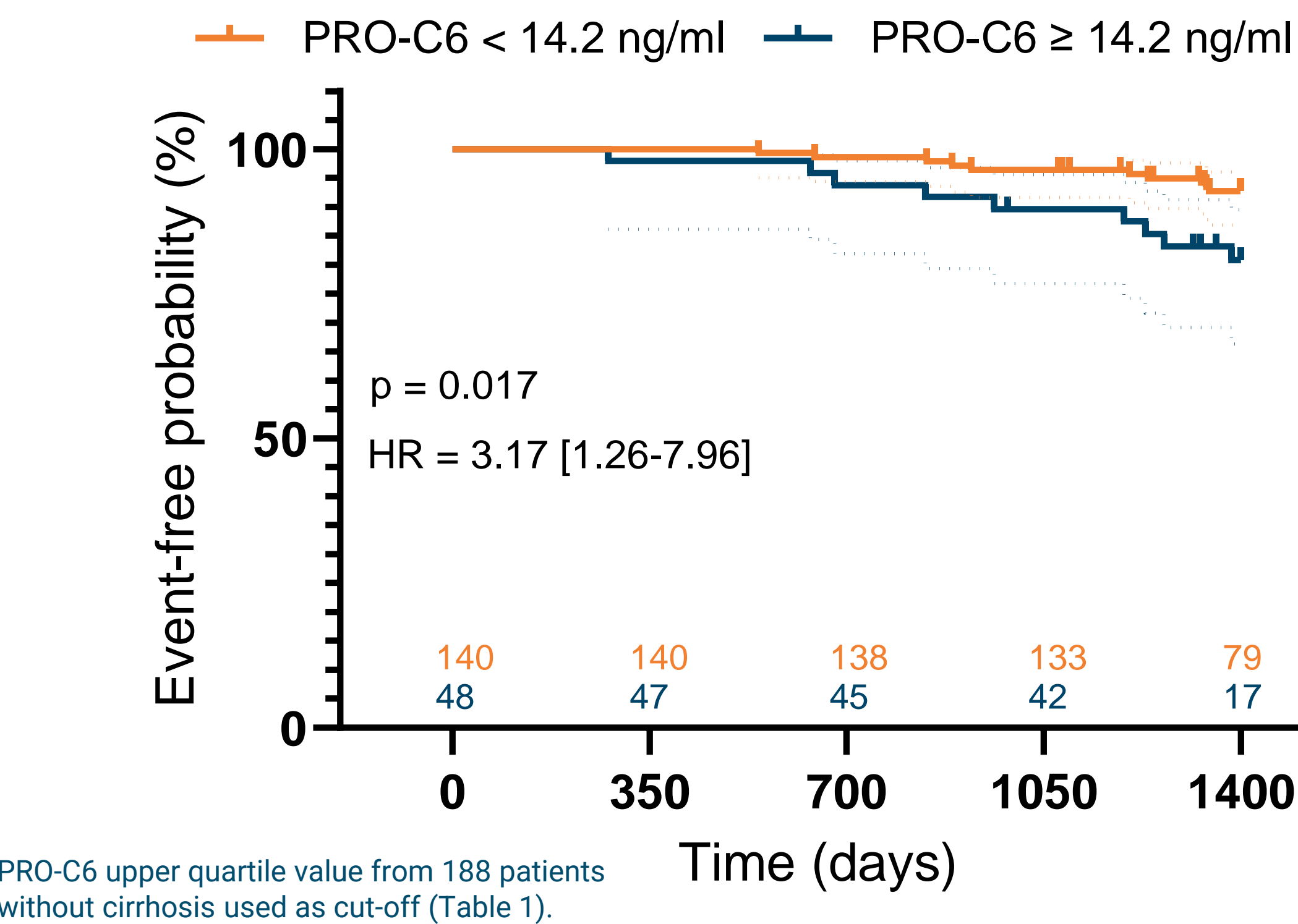
¹ n (%); Median (IQR), ² Pearson's Chi-squared test; Mann-Whitney U test.

RESULTS

In all 339 patients, the hazard ratio for having a liver-related event was 3.08 times higher in patients with high baseline PRO-C6



In 188 patients without cirrhosis, the hazard ratio for having a liver-related event was 3.17 times higher in patients with high PRO-C6



CONCLUSION

- PRO-C6, a biomarker of circulating endotrophin, was primarily associated with an increased risk of developing a liver-related event in patients with cirrhosis from CHC.
- PRO-C6 is a potential monitoring blood-based marker that may also provide prognostic information in treatment-naïve CHC patients with moderate-advanced fibrosis at higher risk of developing a liver-related event.
- The prognostic utility of PRO-C6 in CHC patients after sustained virologic response and other advanced stage chronic liver disease is required.

Subgroup of patients with cirrhosis

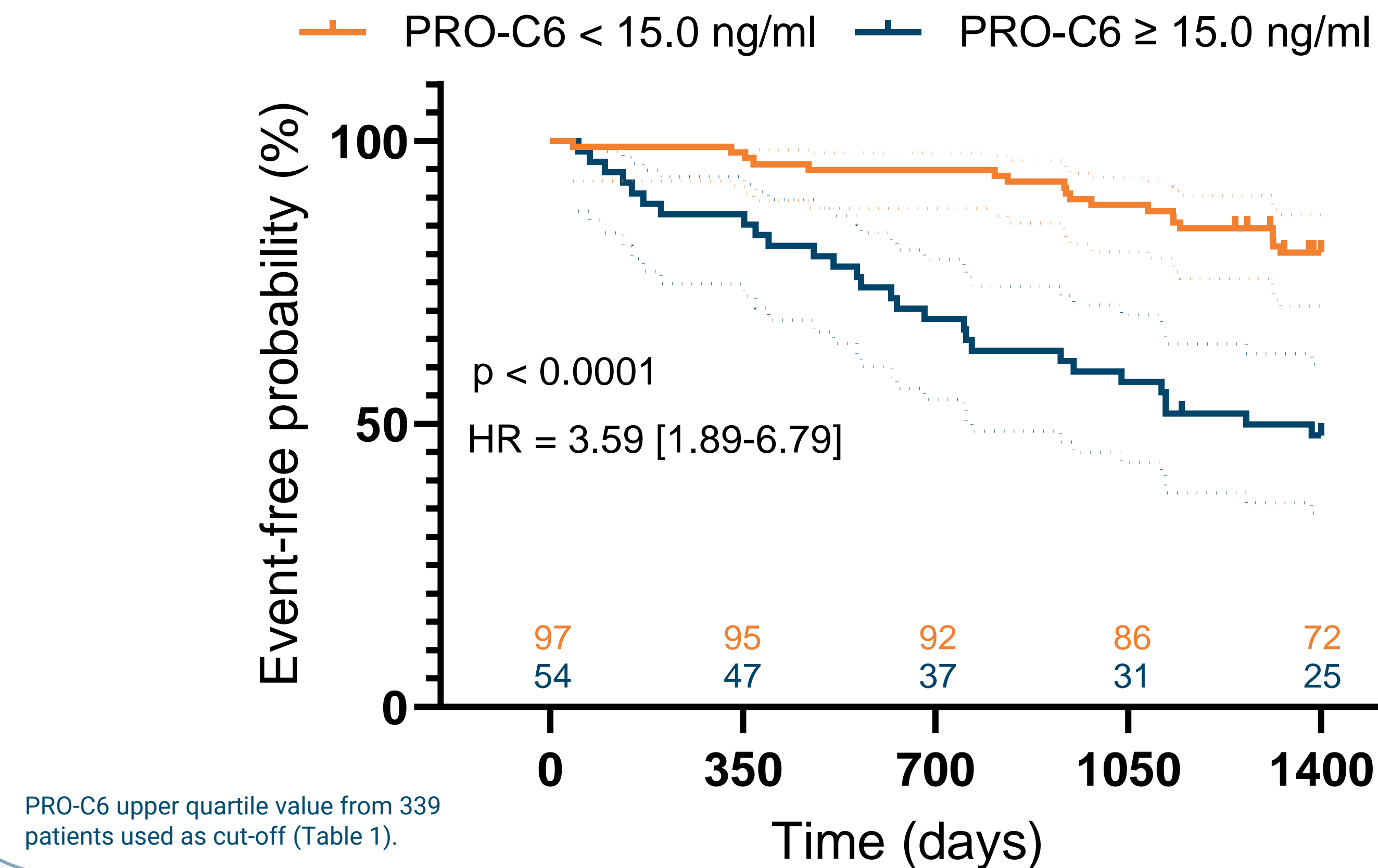
Cirrhosis subgroup demographics

Table 2.

Baseline characteristics	All patients with cirrhosis, N = 151 ¹	No liver-related event, N = 104 ¹	Liver-related event, N = 47 ¹	p-value ²
Sex, female	47 (31%)	30 (29%)	17 (36%)	0.4
AGE, years	50 (47, 55)	51 (47, 55)	50 (47, 54)	0.4
BMI, kg/m2	29.3 (26.7, 32.6)	29.0 (25.9, 31.5)	30.6 (27.8, 33.8)	0.021
Alcohol consumption, life drinks	7,808 (1,411, 23,574)	7,843 (1,291, 21,595)	6,967 (1,790, 34,930)	0.4
ALT, U/L	90 (65, 133)	99 (64, 134)	83 (68, 125)	0.5
PRO-C6, ng/mL	13.3 (10.7, 17.2)	12.2 (10.5, 15.0)	16.6 (11.6, 18.8)	<0.001

¹ n (%); Median (IQR), ² Pearson's Chi-squared test; Mann-Whitney U test.

In 151 patients with cirrhosis, the hazard ratio for having a liver-related event was 3.59 times higher in patients with high PRO-C6



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Disclosures: TW, ES, MK, and DJL are employed at Nordic Bioscience. MK and DJL are shareholders.